

REMARKS

Reconsideration and withdrawal of the rejections of the May 17, 2006 Office Action is respectfully requested in view of the amendments and remarks herein. The Examiner is thanked for the many courtesies extended during the May 24, 2006 personal interview.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 1-3, 5-7, 9-32 and 65 are now pending. Claims 1, 2, 7, 10-21 and 65 have been amended, and claims 4 and 66 have been cancelled, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is submitted that these claims are and were in full compliance with the requirements of 35 U.S.C. §112. In addition, the amendment and remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112; but rather the amendments and remarks herein are made simply to round out the scope of protection to which Applicant is entitled.

II. THE OBJECTION TO THE TITLE IS OVERCOME

The Office Action stated that the title of the invention was not descriptive and should be amended. The title has been amended herewith, and it is believed that the title is now fully descriptive. Accordingly, reconsideration and withdrawal of the objection to the title is respectfully requested.

III. THE REJECTIONS UNDER 35 U.S.C. §112 ARE OVERCOME

Claim 66 was rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The rejection is respectfully traversed.

Claim 66 has been cancelled by the amendment herein, such that the rejection is now moot. Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph is respectfully requested.

Claims 7, 21 and 66 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

Specifically, claim 7, which was previously dependent on claim 2, recited “each of R₃ and R₄ is H,” however claim 2 allegedly lacked identification and definition of said groups. Claim 21 was allegedly missing the identity of the 4-substituent of formula VI and a period at the end. Claim 66 allegedly was not clear in describing what was encompassed within “treating endocrine-dependent cancers.”

As described above, claim 66 has been cancelled herein, rendering the rejection moot as to claim 66. Furthermore, claim 7 has been amended herein, such that claim 7 now depends from claim 3, which claim contains the identification and definition of groups R₃ and R₄, such that the rejection of claim 7 is now moot.

Turning to the rejection of claim 21, the amendment herewith adds a period to the claim. However, it is believed that the claim as previously pending fully contained the possible 4-substituents of formula VI, and respectfully request clarification from the Examiner if the Examiner disagrees.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are respectfully requested.

IV. THE OBJECTION TO DUPLICATE CLAIMS IS OVERCOME

Claim 4 was objected to as being a substantial duplicate of claim 1. Claim 4 has been cancelled herein, rendering this objection moot. Accordingly, reconsideration and withdrawal of the objection to claim 4 is respectfully requested.

V. THE DOUBLE PATENTING REJECTIONS ARE OVERCOME

Claims 32, 65 and 66 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-9 of U.S. Patent No. 5,830,886. Claims 1-7 and 9-32 were rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-48 of U.S. Patent No. 6,903,084. Claims 1-7, 11-20, and 22-31 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 71-80 and 84 of co-pending application

number 10/367,114. Claims 1-7, 11-20, 22-31, 32, 65 and 66 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-12 of co-pending application number 10/955,962.

The Office Action states that while the pending claims are not identical to those of the cited patents and applications, the present claims are obvious as the cited patents and applications allegedly encompass the inhibition of steroid sulphatase utilizing similar substituted 3-sterol sulphamates and/or steroid sulphamates having substitution on the A-ring.

A finding of obviousness-type double patenting turns on whether the invention defined in a claim in the application in issue is an obvious variation of the invention defined in a claim of a prior patent. *See, e.g., In re Berg*, 46 U.S.P.Q.2d, 1226 (Fed. Cir. 1998). In order for an obviousness-type double patenting rejection to stand, the Examiner must show that the claims in this application are obvious **based solely on the claims in the prior patent**; the disclosure in the prior patent cannot be used as prior art.

When comparing the claims of the cited co-pending applications and issued patents to the claims of the instant application, the double patenting rejection should be withdrawn. Nowhere is there a teaching of a compound having a steroidal ring structure having a sulphamate substituent on the A-ring and at least one other substituent at one or more of the 2- and 4-positions, wherein the 2- and 4-positions cannot both be H.

The instant invention is directed to *inter alia*, compounds having a steroidal ring structure with a sulphamate substituent on the A-ring, wherein the compounds have at least one other substituent at one or more of the 2- and 4-positions, wherein the 2- and 4-positions cannot both be H. The instant application has identified that these compounds provide advantages over the steroidal sulphamate compounds known in the art. More specifically, as described *infra*, Purohit *et al.* (enclosed) demonstrates that the claimed A-ring modified compounds are potent inhibitors of steroid sulphatase that do not stimulate uterine growth, in contrast to compounds such as oestrone-3-*O*-sulphamate (EMATE).

None of the claims of the cited patents or co-pending applications cited by the Examiner teach or suggest the advantages associated with the substitution on the A-ring in at least one of the 2- or 4-positions. The skilled person reading the claims of the cited references would therefore not be motivated to produce a steroidal ring structure with a sulphamate substituent on the A-ring, wherein the compounds have at least one other substituent at one or more of the 2-

and 4-positions, wherein the 2- and 4-positions cannot both be H, with the expectation of obtaining a compound having improved properties, including the lack of stimulation of uterine growth.

Accordingly, the claims of the cited patents and co-pending applications do not disclose, teach or suggest the instant claims.

As the requisite teaching, suggestion, incentive and motivation are absent from the claims of the cited patents and co-pending applications, the obviousness-type double patenting rejection must fail as a matter of law.

Accordingly, reconsideration and withdrawal of the double patenting rejections are respectfully requested.

VI. THE ART REJECTIONS ARE OVERCOME

Claims 1-7, 9-32, 65 and 66 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Reed *et al.* (WO 93/05064). The rejection is respectfully traversed.

The Office Action states that Reed *et al.* teaches steroid sulphatase inhibitors and their use in the treatment of estrogen dependent cancers. The Office Action admits that the present invention is different than the teachings of Reed *et al.* in that the present invention claims A-ring substituted derivates. However, the Office Action concludes that it would have been obvious to utilize any of the species of the genus taught by Reed *et al.*, including the claimed compounds. Applicants respectfully disagree.

Initially, in determining whether claims are obvious in view of a reference, it is well-settled that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Further still, "obvious to try" is not the standard under 35 U.S.C. §103. *In re Fine*, 5 U.S.P.Q. 2d 1596, 1599 (Fed. Cir. 1988). And, as stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." Also, for an obviousness rejection to stand, **both the suggestion of the claimed invention and the expectation of success must be founded in the**

prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Furthermore, the Examiner is respectfully reminded that a species (or subgenus) may be patentably distinct from a genus. *See e.g., In re Baird*, 29 U.S.P.Q.2d 1550, 1551 (Fed. Cir. 1994) ("The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious."). *See also In re Jones*, 21 U.S.P.Q.2d 1941, 1943 (Fed. Cir. 1992) (rejecting Commissioner's argument that "regardless .. how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it").

Indeed, mention is also made of the Commentary to Rules of Practice, 49 Fed. Reg. 48416, 48433 (Dec. 12, 1984), 1050 O.G. 395 (Jan. 29, 1985), corrected to 50 Fed. Reg. 23122 (May 31, 1985), 1059 O.G. 27 (Oct. 22, 1985), which provides in pertinent part:

Thus, if a species is patentable over a genus, the species is a "separate patentable invention" from the genus. Compare *In re Taub*, 348 F.2d 556, 146 USPQ 384 (C.C.P.A., 1965).

In this regard, the Examiner's attention is also directed to *In re Sasse*, 207 U.S.P.Q. 107 (C.C.P.A. 1980), wherein the Court of Customs and Patent Appeals held that a claim to a genus and a claim to a species within the genus are not claims to the same or substantially the same subject matter in the sense of 35 U.S.C. §135(b).

In the instant case, the present claims are a patentable species with the genus taught by *Reed et al.*

Reed et al. teaches polycyclic compounds having a sulphamyl or substituted sulphamyl group, preferably at the 3-position. Although *Reed et al.* mentions that substituted polycyclic compounds could be used in the invention, there is no teaching or suggestion in *Reed et al.* that would prompt one of skill in the art to select a compound having substitutions on the A-ring at one or more of the 2- or 4-positions over any of the other compounds included in the genus taught by *Reed et al.* Furthermore, there is certainly nothing in *Reed et al.* that suggests that such a selection of an A-ring substituted derivate would have surprisingly superior properties to that of compounds such as EMATE, as has now been proven.

To this end, enclosed is a copy of Purohit *et al.* "The Development of A-ring Modified Analogues of Oestrone-3-O-sulphamate as Potent Steroid Sulphatase Inhibitors with Reduced Oestrogenicity," published in 1998. As is described in Purohit, one of the problems in the art surround the use of standard steroid sulphatase inhibitors such as EMATE is that the compounds

have a stimulatory effect on uterine growth. Such a stimulatory effect is undesirable in potential therapies for diseases such as cancer.

Surprisingly, it has now been found that the A-ring modified compounds of the present invention, having at least one additional substituent at one or more of the 2- and 4-positions, are vastly superior to previous steroid sulphatase inhibitors. Specifically, the A-ring modified compounds exhibit steroid sulphatase inhibition with significantly decreased estrogenicity when compared to compounds such as EMATE. For example, the Examiner's attention is respectfully directed to Figure 4, which compares *in vivo* sulphatase activity following administration of 2- or 4-position substituted derivatives or EMATE. The sulphatase activity measured following administration of compounds such as 4-Nitro EMATE, 2-Methoxy EMATE, and 4-n-Propyl EMATE was statistically similar to the activity levels measured following administration of EMATE. Furthermore, Figure 5 depicts the results of the uterine growth assay, which demonstrates that administration of A-ring derivative compounds resulted in little or no uterine growth, in contrast to the effects of the administration of EMATE.

Accordingly, the present invention is patentable over Reed *et al.* as there is no suggestion, motivation, or teaching in Reed *et al.* that would prompt one of skill in the art to select the compounds of the present invention from the numerous compounds of the genus described by Reed *et al.* Furthermore, the present invention is additionally patentable over Reed *et al.* as there is no suggestion, motivation, or teaching in Reed *et al.* that would suggest to one of skill in the art that the compounds of the present invention would possess surprisingly advantageous properties that are lacking from traditional steroid sulphatase inhibitors. For all of these reasons, reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) over Reed *et al.* is respectfully requested.

Claims 2, 3, 9, 10 and 32 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Prezewowsky *et al.* (US 3,951,959). The rejection is respectfully traversed.

The Office Action alleged that Prezewowsky *et al.* taught 1,3-oxygenated 8 α -estratrienes such as 1,3-bis(diethylaminosulfonyloxy)-8 α -estra-1,3,5(10)-trien-17-one, of which the compounds in claim 2, 3, 9, 10 and 32 were positional isomers, and were therefore obvious over the teachings of Prezewowsky *et al.*

Applicants note that claim 11, as previously presented, was not rejected over Prezewowsky *et al.* as claim 11 required that R₁ and R₂ cannot both be H. It is respectfully

submitted that this recitation has been added to claim 2 via the amendment herein, such that the compound of claim 2 cannot have both R₁ and R₂ being H, and the compound is therefore not a positional isomer of the compounds taught by Prezewowsky *et al.* Similarly, claim 1 has also been amended to recite that R₁ and R₂ cannot both be H. As all of the rejected claims depend from either claim 1 or claim 2, the amended recitations ensure that none of the rejected claims now describe a compound where both R₁ and R₂ can simultaneously be H, and the claims are therefore not obvious over Prezewowsky *et al.*

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) over Prezewowsky *et al.* is respectfully requested.

VII. OTHER MATTERS

Applicant was required to provide a list of all patents and co-pending applications which may contain overlapping subject matter. Applicants have included below an Information Disclosure Statement providing a listing of all related patents and co-pending applications. It is respectfully believed that this submission satisfies the requirement of the Office Action.

The Office Action suggested that the header "Brief Description of the Drawings" be inserted into the specification. Applicants have amended the specification herein accordingly, such that the heading has been inserted in the specification.

VIII. INFORMATION DISCLOSURE STATEMENT

The Examiner's attention is respectfully directed to the following documents set forth in the accompanying form PTO-1449, which is provided in duplicate. A copy of the cited documents is enclosed. Applicants request that the Examiner consider and make of record the documents cited herein and that the Examiner return an initialed copy of the Form PTO-1449 to the Applicant's attorneys. As stated above, the Information Disclosure Statement includes all patents and co-pending applications which may contain overlapping subject matter. The inclusion of any patent or application on the Information Disclosure Statement is not an indication that Applicants consider the patent or application to contain subject matter which overlaps with that of the present invention.

This Information Disclosure Statement is not a representation that the documents cited herein is considered most pertinent, or that a search has been undertaken or that the cited documents are indeed prior art. The Examiner is invited to undertake an independent search.

As this Information Disclosure Statement is being submitted after receipt of a non-final Office Action, the Commissioner is hereby authorized to charge the required fee of 180.00 to Deposit Account 50-0320.

As these documents present no new issues to patentability, it is respectfully requested that the Examiner considers and make of record the documents cited herewith and that a copy of Form PTO-1449 be initialed by the Examiner and returned to the undersigned.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, prior to issuance of any paper other than a Notice of Allowance, a further interview, is respectfully requested, with the Examiner and her supervisor, and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks made herewith, the application is in condition for allowance. Favorable reconsideration of the application, and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date.

Respectfully submitted,
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